Developing strategies for effective international trial management
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Practical planning for the Clinical Trial Lifecycle: “Expect the best, plan for the worst, and prepare to be surprised.”

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The numbers may vary by source, but there is widespread agreement that most clinical trials experience significant delays during their life cycle. Variable expenses increase with every month the trial timelines are extended and the delay of product launches could mean the loss of millions of dollars in potential revenue.

Clinical trial planning and execution is one of the most complex project management activities in any industry, involving timelines spanning across years, multiple vendors and contributors, tens of millions of dollars, and variables often beyond the control of the sponsor. Every trial is different, the landscape keeps evolving, and there are always surprises. How do you plan appropriately for the successful execution of clinical trials knowing that you will experience unexpected barriers and delays? How do you manage the expectations of investors and Board members who want you to go faster while spending less?

There is no single approach that works best. However, there are guiding principles that will help focus your planning efforts and outputs.

- Planning never ends; it evolves and adjusts.
- Planning needs an owner.
- Planning requires performance measures, escalation and timely decision making.
- Planning must be realistic and transparent.

These tenets apply throughout the clinical trial life cycle with emphasis depending on study stage and audience for the information.

There are three common themes related to delays that we see in virtually every clinical trial and should be addressed in the planning process.

1. Getting out of the gate late. Start up delays during site selection, regulatory document completion, and institutional contract/committee approvals are a very common source of frustration for the study team.

2. Clinical Drug Supply putting the brakes on study start. In the words of Roseanne Roseannadanna: “It’s always something.” Drug supply shortages, insufficient documentation for QP release, importation restrictions and customs barriers are just a few examples.

3. Enrolment off track. There are a number of root causes of enrolment delays, including impractical protocol design elements and low/non-enrolling sites.

These issues are not easily avoided via quick fixes, but understanding, measuring, and assessing the operational risks will allow you to develop proactive strategies and timely contingency plans.

In this article, we include our top five tips for planning in each of the stages leading up to study start up. While the strategies and processes related to vendor selection and investigational product supply chain management are critical, many articles have addressed these topics in detail, so we will only touch on them briefly.

Planning for funding

As a sponsor seeking investors (or budget approval), it is a fine balance between defining high level scientific and protocol...
strategy while accounting for operational cost drivers to develop a realistic budget forecast. Most sponsors underestimate the cost of clinical research and end up requesting additional funding later. How do you avoid this pitfall with limited resources and, often, minimal or no experience with trial execution?

There is a temptation at this stage to make premature decisions regarding study design, regional involvement, and start up timelines. While the pressure to commit to deliverables is significant, we caution sponsors against putting the cart before the horse. The critical outputs at this stage are a draft cross-functional Clinical Study Plan, preliminary budget forecast, and strategy for outsourcing. Get expert input and start with the end in mind. Know where you want to go before proceeding to the next stage because you need to be prepared to answer many questions from vendors who want to help you refine your plan moving forward.

**Top 5 guidance points for planning for funding**

1. Assign an experienced project manager as owner of the cross functional plan.
2. Consult with experts and get a second opinion where necessary – scientific and medical advisors, regulatory agencies, biostatistics, and clinical operations teams. Ensure team members and roles are clearly defined.
3. Ensure your investigational product manufacturing, sourcing and timelines are in order.
4. Educate yourself and your Board of Directors/investors about clinical research, ICH E6 sponsor obligations, and manage expectations.
5. Use benchmarks for budgeting - tap into modeling and planning tools from experts and/or vendors who will identify key budget drivers and draw on extensive data sources.

**Planning for decision making**

This stage is extremely busy and may span many months, which is why it is critical to have your sponsor and virtual expert team well-defined. Key deliverables include a protocol synopsis leading to a draft protocol.
regulatory meetings, and RFPs for vendors. You should have a good grasp of the activities on the critical path for study start up. There is a lot of input and data to discuss and review before finalizing the protocol and related plans, selecting vendors, and making decisions about operational design.

Top 5 guidance points for planning for decision making

1. Ensure your sample size accounts for screen failures, dropouts, endpoint ineligible patients, and loss to follow up.
2. Develop a potential vendor list focusing on track record and fit. Send out a well-defined RFP, including expectations, roles and responsibilities. Seeking input from experts and vendors will be an iterative process as you incorporate data from multiple sources.
3. Work with potential CROs to design feasibility. Speak to potential sites in addition to reviewing feasibility questionnaire data. Be open, realistic, and flexible about region and site selection strategies.
4. Develop a Risk Mitigation Plan.
5. Allow at least six months to ensure investigational, companion, and comparator products are ready for packaging, labeling, distribution, and importation.

Planning for execution

You are now preparing for study start up. Vendors are selected, contracts signed, and team members assigned. The protocol is final and many operational documents will be drafted for regulatory submissions and study management. Your expert team should be prepared for decisions that require your input and approval. You may need to refine feasibility assessments if the protocol has changed significantly since the draft.

Top 5 guidance points for planning for execution

1. Carefully review and approve proposed team member qualifications and experience, especially vendor Project Managers and CRAs.
2. Establish team communication, roles and responsibilities related to reviews and approvals. Have clear expectations for deliverables.
3. Develop the Quality Oversight Plan.
4. Develop a Dashboard based on the communication needs of the Board and investors. Identify the various sources of trial performance data and develop your analytics process. Measure what matters.
5. If your study is blinded, define the unblinded team member(s) on the sponsor side and at all vendors and ensure communication and escalation processes are documented.

As you execute your trial, you will encounter some of the barriers you identified in your Risk Mitigation Plan and maybe some that will surprise you. Defining and assessing performance measures and implementing sponsor oversight early will allow the team to trigger contingency plans and adjust course. There are no guarantees in drug development, but thoughtful planning and smart execution can improve the likelihood of your clinical trial's operational success.

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\[1\] Denis Waitley, motivational speaker and author
\[2\] Cutting Edge Information, “Clinical Operations Benchmarking Per-Patient Costs, Staffing and Adaptive Design,” 2011